August 9, 2001

David Brandwene, Ph.D.
Senior Toxicologist
Akzo Nobel Chemicals Inc.
5 Livingstone Ave.
Dobbs Ferry NY 10522

Dear Dr. Brandwene,

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Tris(1,3-dichloro-2-propyl) phosphate (Fyrol FR-2, CAS No.13674-87-8), transmitted to EPA March 20, 2001. I commend Akzo-Nobel for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA agrees with Akzo-Nobel's conclusion that for priority-setting purposes no new reproductive toxicity tests are necessary, but our reasoning is different, as explained in the comments.

The Company needs to supply critical information missing from the ecotoxicity robust summaries and clarifications to certain health and environmental fate robust summaries.

As with other submissions where the available data are either inadequate or insufficiently documented, this case will remain open until adequate documentation is in hand.

EPA will post this letter and the attached Comments on the Chemical RTK web site within the next few days. As noted in the comments, we ask that Akzo-Nobel advise the Agency, within 60 days of the posting on the Chemical RTK website, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-260-3470. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
C. Auer
M. E. Weber
A. Abramson

EPA Comments on Chemical RTK HPV Challenge Submission: Tris(1,3-dichloro-2-propyl) phosphate

SUMMARY OF EPA COMMENTS

The sponsor, Akzo Nobel Functional Chemicals LLC, submitted a Test Plan to EPA, transmitted March 20, 2001, for Tris(1,3-dichloro-2-propyl) phosphate (Fyrol FR-2, CAS No.13674-87-8). EPA posted the submission on the ChemRTK HPV Challenge Web site on April 6, 2001.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical and Environmental Fate Data. EPA agrees with the test plan for these endpoints. However, clarification is needed in regard to the citations used for the partition coefficient data (see Test Plan and Robust Summary below). Clarification is also needed in regard to the hydrolysis of this chemical at pH 9 (see Test Plan and Robust Summary comments below).

2. Health Endpoints: All appropriate SIDS health endpoints have been addressed. While the reproductive toxicity study is judged inadequate, the combination of the 90-day and developmental studies adequately addresses this endpoint. Several robust summaries need to be enhanced for clarity (see specific comments below).

3. Ecotoxicity. Some required data elements were missing for all three ecological endpoints (fish, daphnid, algae), and EPA therefore reserves judgement on the adequacy of these studies pending submission of missing data elements.

EPA requests that the Sponsor advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE TRIS(1,3-DICHLORO-2-PROPYL) PHOSPHATE CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

EPA agrees with the submitter's test plan for these endpoints; however, in regard to partition coefficient, the submitter should provide source information for literature data (See Robust Summary comments below).

It is important that these endpoints be measured experimentally, as accurate information on, for example, vapor pressure will help evaluate the ecotoxicity data.

Environmental Fate (photodegradation, stability in water, biodegradation, and transport/distribution).

EPA agrees with the submitter's test plan for these endpoints.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate existing data are available for all these endpoints. EPA agrees with the conclusions of the sponsor that no new reproductive toxicity tests are necessary, but for different reasons. EPA believes the reproductive toxicity study submitted does not satisfy the SIDS-level assessment for this endpoint (see below for specific comments). However, current OECD SIDS policy states that an existing 90-day study with evaluation of male reproductive organs plus a developmental toxicity study, both of which are available for Fyrol FR-2, satisfy the reproductive toxicity endpoint for a screening-level (SIDS-level) analysis.

Ecological Effects.

EPA reserves judgement on data adequacy for all ecological endpoints pending the outcome of the vapor pressure test and submission of missing data elements from the ecological robust summaries (see Robust Summary comments below).

SPECIFIC COMMENTS ON ROBUST SUMMARIES

Chemistry

Partition Coefficient

One of the submitter's two calculated values is similar to the two it quoted from the literature (the submitter failed to specify the source of the literature values–a deficiency in the summary). The submitter states that the literature values' validity could not be confirmed because the original citations were not available. However, EPA found literature log P values of 3.65 (Inspection and Testing Institute; "Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan", Japan Chemical Industry Ecology-Toxicology and Information Center; ISBN # 4-89074-101-1 (1992)) and 3.76 (Sasaki K et al.; Bull. Environ. Contam. Toxicol. 27: 775-82 (1981); cited in Hazardous Substances Data Bank, National Library of Medicine, http://toxnet.nlm.nih.gov). These values appear to correspond to the sponsor's literature values, and the Sasaki reference, at least, should be readily accessible. The sponsor needs to examine readily available reports of measured data and amend its robust summary accordingly.

Fate

Stability in Water (Hydrolysis)

The submitter indicated that Fyrol FR-2 is hydrolytically stable under acid and neutral conditions, with some instability shown at pH 9. The submitter's linear regression analysis reports a half life of 120 days at pH 9 and 20 °C, which seems to be inconsistent with the observed data (96.1 % recovery of parent in 30 days). EPA recommends that the submitter review its calculations, and if necessary to recalculate the half life of this chemical at pH 9 and 20 °C.

Health Effects

EPA has the following comments on the robust summaries for health endpoints for Fyrol FR-2:

Repeat dose toxicity: In the summary of a combined chronic toxicity/carcinogenicity study in rats, the incidence by dose for all noncarcinogenic effects needs to be provided.

Genetic toxicity: The "In vitro mammalian cell gene mutation test" summary includes results of three endpoints in one study: (1) gene mutation; (2) sister chromatid exchanges; and (3) chromosomal aberrations. *Each of these should be summarized as separate reports*. The following information needs to be provided for each one: (1) method details (especially for the chromosomal endpoints such as number of metaphases analyzed, and the number of SCEs per cell and per chromosome for SCE assay, and criteria for scoring); and (2) the incidence by dose for the results of the SCE and chromosomal aberration studies.

Reproductive Toxicity: The submitted reproductive toxicity study is considered inadequate because: (1) rabbits are not the preferred species for the reproductive toxicity study; and (2) only male rabbits were evaluated.

Developmental Toxicity: The incidence by dose for all effects needs to be provided. In addition, based on the increased incidence of resorptions, decreased incidence of fetal viability, decreased mean fetal weight and length, and delayed skeletal development seen at 400 mg/kg/day, the

NOAEL for developmental toxicity should be identified as 100 mg/kg/day.

Ecotoxicity Studies

The comments below reflect the information presented in the robust summaries; information in the full study report may address some of the issues identified.

Acute Aquatic Toxicity. Robust summaries were submitted for studies on fish, daphnia, and green algae. Many critical experimental details were omitted from the robust summaries. Owing to the many missing data elements in these studies, EPA reserves judgement on data adequacy for these tests until all missing data are submitted. EPA has provided specific comments on how to enhance the robust summaries to the standard established in EPA's HPV Challenge Program guidance at http://www.epa.gov/chemrtk/guidocs.htm.

Fish. Information missing from the robust summary includes: test substance purity, pH, hardness, DO, TOC, TSS, temperature, exposure vessel type (e.g., size, head space, sealed, aeration, lighting), number of replicates, and fish per replicate.

Aquatic Invertebrates. Information missing from the submitted acute daphnid test robust summary includes: test substance purity, pH, hardness, DO, TOC, TSS, temperature, concentration of the vehicle used, and number of organisms per treatment.

Aquatic Plants. Information missing from the robust summary includes: test substance purity, pH, hardness, DO, TOC, TSS, temperature, exposure vessel type (e.g., size, head space, sealed, aeration, lighting).

Followup Activity

EPA requests that the Sponsor advise the Agency within 60 days of any modifications to its submission.